UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
08/253,973	06/03/94	MCBRIDE	W 91875J

12M1/0616
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EXAMINER	
HARTLEY, M	
ART UNIT	**PAPER NUMBER**
1211	16

DATE MAILED: 06/16/97

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 5-13-97.

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-36 is/are pending in the application.

Of the above, claim(s) 11-25, 27, 30 and 32-36 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-10, 26 and 31 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

-- SEE OFFICE ACTION ON THE FOLLOWING PAGES --

★ U.S. GPO: 1996-410-238/40050

Response to Amendment

The amendment filed 5-13-97 has been entered. Claim 2 has been amended.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-10, 26 and 31 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Fritzberg (USP 4,965,392, PTO-1449, dated 6-4-96) in combination with Rhodes (WO/12819, PTO-1449, dated 6-4-96), for the reasons set forth in the office action mailed 11-13-97.

Applicant's arguments filed 5-13-97 have been fully considered but they are not persuasive.

Applicant asserts that the declaration filed by the applicants under 73 CFR 1.131 establishes that the claimed invention was invented prior to 7-8-93. Thus, the Rhodes reference does not qualify as prior art.

The declaration filed on 5-13-97 under 37 CFR 1.131 has been considered but is ineffective to overcome the Rhodes reference.

The evidence submitted is insufficient to establish a reduction to practice of the invention in this country (or a NAFTA or WTO member country, if applicable) prior to the effective date of the Rhodes reference.

The applicants have failed to provide a clear showing of the facts to establish the claimed dated of invention, as set forth in MPEP 715 which states:

> The showing of facts shall be such, in character and weight, as to establish reduction to practice prior to the effective date of the reference, or conception of the invention prior to the effective date of the reference coupled with due diligence from prior to said date to a subsequent reduction to practice or to the filing of the application. Original exhibits of drawings or records, or photocopies thereof, must accompany and form part of the affidavit or declaration or their absence satisfactorily explained.

Applicant has failed to provide any evidentiary documents and discussion of how the documents clearly prove the date of invention. Also, the applicant has not identified that the acts of invention were performed in the U.S. Furthermore, it is noted that the declaration is not executed, i.e., is not signed by the inventors. The 1.131 declaration has been considered, however, since applicant has not provided any of the laboratory notebook records or data as evidence to establish the date and provided a discussion on what the documents prove, the declaration is not deemed persuasive to establish a date of invention prior to the Rhodes reference.

Applicant further asserts that since the Fritzberg reference was asserted in combination with Rhodes, both references are required to assert obviousness. Thus, elimination of the Rhodes reference rebuts the obviousness rejection.

This assertion is not found persuasive. The statement of "Fritzberg in combination with Rhodes" is used to denote an either/or situation, wherein either Fritzberg or Rhodes may be used in the obviousness rejection, but some of the extraneous teachings known in the art (e.g., various targeting moieties or metals) of Rhodes may be used in Fritzberg and *vice versa*. This is clearly evidenced in the combination of the references in the motivation statement in the office action mailed 11-13-96. The office action does not assert or suggest that Rhodes solves some deficiency of the teaching of Fritzberg or *vice versa*. The office action stated "Fritzberg and Rhodes disclose formulae which may be substituted to yield various monoamine, diamide, thiol-containing metal chelating agents, such as, various amino acid sequences which are modified to yield medically useful metal-ion binding domains which may be linked to various specific targeting moieties to gain the advantage providing various reagents which are useful for preparing a radiopharmaceutical agent, which may be specifically targeted to a desired site in vivo for treatment or diagnosis." There is no indication in this statement or anywhere in the office action mailed 11-13-96, which would suggest that one of the references required the other to formulate obviousness. Such a dependent relationship between the references as asserted by the applicant is usually signified with "reference A in view of B." Thus, the Fritzberg reference may stand alone for a *prima facie* case of obviousness over the instant claims.

Applicant asserts that the Fritzberg reference is limited to proteins and not peptides as taught in the instant invention.

This is not found persuasive because the instant claims appear drawn toward a chelator attached to a "targeting moiety" and Fritzberg teaches chelators attached to proteins, wherein the

proteins are clearly within the scope of a targeting moiety. The peptides stated in the claims are part of the chelator and Fritzberg teaches chelators which are within the scope of these claims.

Applicant asserts that the 37 USC 1.132 declaration filed by one of the inventors on 5-13-97 overcomes the obviousness rejection over Fritzberg.

The declaration under 37 CFR 1.132 filed 5-13-97 is insufficient to overcome the rejection of claims 1-10, 26 and 31 based upon Fritzberg as set forth in the last Office action because of the following reasons.

The recitation of "In my opinion, the teachings of this reference would have been understood by one of ordinary skill in the art only in view of the teachings of the specification in its entirety," as set forth in statement No. 5 is vague. It is not clear if "the specification" is referring to the specification of the instant application or the reference patent. This statement is also vague because there is no specific statement of what would have been understood in view of what and because it fails to differentiate the instant invention from the prior art.

The remaining statements in the declaration appear to assert that the Fritzberg reference teaches triamide thiol chelators but does not teach monoamine, diamide thiol chelators or provide a teaching that would provide a reasonable expectation of success in making and using monoamine, diamide thiol chelators. Applicant appears to support these assertions by noting that all of the exemplified chelators disclosed in Fritzberg are triamide thiol chelators.

These assertions are not found persuasive because Fritzberg teaches chelators of the formula shown in column 3, wherein X may be H2 or =O. Substituting one of the X's as H2 and

the others as =O, would yield a monoamine, diamide thiol chelator. Fritzberg also teaches that amino acids comprising various side chains may be employed in the synthesis of the compounds of the invention, see column 8, lines 19-21. This teaching would suggest preparation of entire scope of the disclosed chelators, including monoamine, diamide thiol chelators. Although Fritzberg may not exemplify a monoamine, diamide thiol chelator, such chelators are clearly taught in the specification of Fritzberg, as noted above. A reference as a whole must be considered, e.g., the specification teaches more than its working examples. A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. Merck & Co. v. Biocraft Laboratories , 10 USPQ2d 1843 (Fed. Cir. 1989). Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi,169 USPQ 423 (CCPA 1971). "The use of patents as references is not limited to what the patentees describe as their own inventions or to the problems with which they are concerned. They are part of the literature of the art, relevant for all they contain." In re Heck , 216 USPQ 1038, 1039 (Fed. Cir. 1983) (quoting In re Lemelson , 397 F.2d 1006, 1009, 158 USPQ 275, 277 (CCPA 1968)).

Given the teaching in Fritzberg, it would not require undue experimentation to: 1) modify the exemplified triamide thiol chelator to form a monoamine, diamide thiol chelator, or 2) use such a chelator in the radiopharmaceutical purposes disclosed in the invention.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in

a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. *In re McLaughlin*, 443 F.2d 1392; 170 USPQ 209 (CCPA 1971). In the instant case, Fritzberg teaches chelators having a variable X in which only 2 choices are provided, H2 or =O. Given the teaching that various amino acids with various side chains may be employed in the synthesis of the chelators and the level in the skill in the art at the time of the claimed invention was made with regards to preparing such chelators, preparing monoamine, diamide thiol chelators would have been, 1) contemplated by, and 2) within the capabilities of, the skilled artisan by the disclosure of Fritzberg.

It is also noted that the declaration filed under 37 CFR 1.132 is not executed, e.g., not signed.

For the above stated reasons, said claims are properly rejected under 35 U.S.C. § 103. Therefore, the rejection is adhered to.

Conclusion

No claims are allowed at this time.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

U.S. Patent 5,443,816 (Inventors: Zamora and Rhodes), is made of record because it discloses peptides having a metal-ion binding domain labeled with a medically useful metal and targeting moiety. It is noted that this patent has a filing date of 2-20-92.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Michael Hartley whose telephone number is (703) 308-4411. The examiner can usually be reached on Monday through Friday from 7:30 a.m. to 4:00 p.m. in the eastern time zone. The facsimile numbers for group 1200 are (703) 308-4556 or (703) 305-3592.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John Kight, III, SPE 1211 can be reached on (703) 308-0204.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

Date: 6-12-97

Hartley/

GARY E. HOLLINDEN, PH.D.
PRIMARY EXAMINER
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